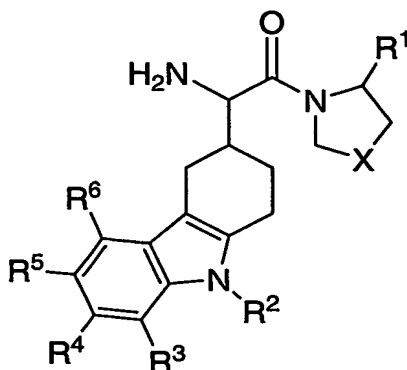


WHAT IS CLAIMED IS:

1. A compound of structural formula I:



I

wherein:

each n is independently 0, 1, 2, or 3;

X is selected from S, S(O), S(O)₂, CH₂, CHF, and CF₂;

R¹ is hydrogen or -CN;

R² is selected from the group consisting of

hydrogen,

C₁₋₆ alkyl, wherein alkyl is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, CO₂H,

C₁₋₆ alkyloxycarbonyl, and

(CH₂)_n-aryl, wherein aryl is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, CO₂H,

C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens;

R³, R⁴, R⁵, and R⁶ are each independently selected from the group consisting of

hydrogen,

halogen,

cyano,

hydroxy,

C₁₋₆ alkyl, wherein alkyl is unsubstituted or substituted with one to five halogens,

C₁₋₆ alkoxy, wherein alkoxy is unsubstituted or substituted with one to five halogens,

(CH₂)_n-COOH,

(CH₂)_n-COOC₁₋₆ alkyl,

(CH₂)_n-CONR⁷R⁸,

(CH₂)_n-NR⁷R⁸,

(CH₂)_n-NR¹⁰SO₂R⁹,

(CH₂)_n-NR¹⁰CONR⁷R⁸,

(CH₂)_n-NR¹⁰COR¹⁰,

(CH₂)_n-NR¹⁰CO₂R⁹,

(CH₂)_n-aryl, wherein aryl is unsubstituted or substituted with one to five substituents

independently selected from halogen, hydroxy, CO₂H,

C₁₋₆ alkyloxycarbonyl, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, and C₁₋₆ alkoxy, wherein alkyl and

alkoxy are unsubstituted or substituted with one to five halogens,

wherein any methylene (CH₂) carbon atom in R³, R⁴, R⁵, and R⁶ is unsubstituted or substituted

with one to two groups independently selected from halogen, hydroxy, and C₁₋₄ alkyl

unsubstituted or substituted with one to five halogens;

R⁷ and R⁸ are each independently selected from the group consisting of

hydrogen,

(CH₂)_n-phenyl,

(CH₂)_n-C₃₋₆ cycloalkyl, and

C₁₋₁₀ alkyl,

wherein alkyl is unsubstituted or substituted with one to five halogens and wherein phenyl and

cycloalkyl are unsubstituted or substituted with one to five substituents independently

selected from halogen, hydroxy, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy

are unsubstituted or substituted with one to five halogens; or

R⁷ and R⁸ together with the nitrogen atom to which they are attached form a heterocyclic ring selected

from azetidine, pyrrolidine, piperidine, piperazine, and morpholine wherein said heterocyclic ring is

unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy,

C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five

halogens;

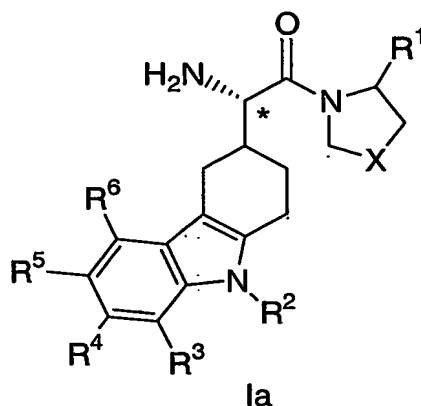
R⁹ is selected from the group consisting of (CH₂)_n-phenyl, (CH₂)_n-C₃₋₆ cycloalkyl, and C₁₋₆ alkyl,

wherein alkyl is unsubstituted or substituted with one to five halogens and wherein phenyl and cycloalkyl

are unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C₁₋₆ alkyl, and C₁₋₆ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens, and wherein any methylene (CH₂) carbon atom in R⁹ is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C₁₋₄ alkyl unsubstituted or substituted with one to five halogens; and

each R¹⁰ is hydrogen or R⁹.

2. The compound of Claim 1 of structural formula Ia wherein the carbon atom marked with an * has the stereochemical configuration as depicted in formula Ia:



3. The compound of Claim 1 wherein X is S, S(O), or S(O)₂.

4. The compound of Claim 3 wherein R¹ is hydrogen.

5. The compound of Claim 2 wherein X is S, S(O), or S(O)₂.

6. The compound of Claim 1 wherein X is CH₂, CHF, or CF₂.

7. The compound of Claim 6 wherein R¹ is hydrogen.

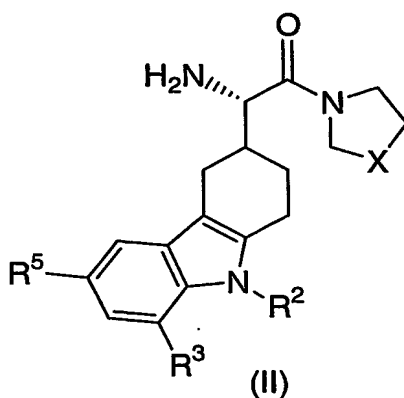
8. The compound of Claim 2 wherein X is CH₂, CHF, or CF₂.

9. The compound of Claim 1 wherein R^2 is hydrogen, methyl, or phenyl.

10. The compound of Claim 9 wherein R^3 , R^4 , R^5 and R^6 are each independently selected from the group consisting of hydrogen, halogen, trifluoromethyl, trifluoromethoxy, carboxy, and
5 COOC₁₋₄ alkyl.

11. The compound of Claim 10 wherein R^4 and R^6 are hydrogen.

12. The compound of Claim 11 of structural formula II selected from the group
10 consisting of:



| <u>X</u> | <u>R²</u> | <u>R³</u> | <u>R⁵</u> |
|-----------------|----------------------|----------------------|----------------------|
| S | H | H | Cl |
| CH ₂ | H | H | Cl |
| CH ₂ | H | H | OCF ₃ |
| CH ₂ | H | H | CF ₃ |
| CH ₂ | H | CO ₂ H | H |
| CH ₂ | H | CO ₂ Et | H |
| CH ₂ | H | H | CO ₂ H |
| CH ₂ | H | H | CO ₂ Et |
| CH ₂ | H | CF ₃ | H |
| CF ₂ | H | CONH <i>n</i> -Dec | H |
| CH ₂ | Me | H | H |
| CH ₂ | Ph | H | H |

13. A pharmaceutical composition which comprises a compound of Claim 1 and a pharmaceutically acceptable carrier.

14. A method for treating diabetes in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

15. A method for treating non-insulin dependent (Type 2) diabetes in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

16. A method for treating hyperglycemia in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

17. A method for treating obesity in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

18. A method for treating one or more lipid disorders selected from the group of dyslipidemia, hyperlipidemia, hypertriglyceridemia, hypercholesterolemia, low HDL and high LDL in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

19. A method for treating in a mammal in need thereof one or more conditions selected from the group consisting of (1) hyperglycemia, (2) low glucose tolerance, (3) insulin resistance, (4) obesity, (5) lipid disorders, (6) dyslipidemia, (7) hyperlipidemia, (8) hypertriglyceridemia, (9) hypercholesterolemia, (10) low HDL levels, (11) high LDL levels, (12) atherosclerosis and its sequelae, (13) vascular restenosis, (14) irritable bowel syndrome, (15) inflammatory bowel disease, including Crohn's disease and ulcerative colitis, (16) other inflammatory conditions, (17) pancreatitis, (18) abdominal obesity, (19) neurodegenerative disease, (20) retinopathy, (21) nephropathy, (22) neuropathy, (23) Syndrome X, (24) ovarian hyperandrogenism (polycystic ovarian syndrome), and other disorders where insulin resistance is a component, wherein the method comprises the administration to the mammal a therapeutically effective amount of a compound of Claim 1.

20. The pharmaceutical composition of Claim 13 further comprising one or more additional active ingredients selected from the group consisting of:

(a) a second dipeptidyl peptidase IV inhibitor;
(b) an insulin sensitizer selected from the group consisting of a PPAR γ agonist, a PPAR α/γ dual agonist, a PPAR α agonist, a biguanide, and a protein tyrosine phosphatase-1B inhibitor;

- 5 (c) an insulin or insulin mimetic;
(d) a sulfonylurea or other insulin secretagogue;
(e) an α -glucosidase inhibitor;
(f) a glucagon receptor antagonist;
(g) GLP-1, a GLP-1 mimetic, or a GLP-1 receptor agonist;
10 (h) GIP, a GIP mimetic, or a GIP receptor agonist;
(i) PACAP, a PACAP mimetic, or a PACAP receptor agonist;
(j) a cholesterol lowering agent such as (i) HMG-CoA reductase inhibitor, (ii) sequestrant, (iii) nicotinyl alcohol, nicotinic acid or a salt thereof, (iv) PPAR α agonist, (v) PPAR α/γ dual agonist, (vi) inhibitor of cholesterol absorption, (vii) acyl CoA:cholesterol acyltransferase inhibitor, and
15 (viii) anti-oxidant;
(k) a PPAR δ agonist;
(l) an antiobesity compound;
(m) an ileal bile acid transporter inhibitor;
(n) an anti-inflammatory agent; and
20 (o) an antihypertensive agent.

21. The pharmaceutical composition of Claim 20 wherein the PPAR α/γ dual agonist is KRP-297.

25 22. A method of treating diabetes in a mammal in need thereof comprising administering to the mammal a therapeutically effective amount of a compound of Claim 1 in combination with the PPAR α/γ dual agonist KRP-297.

30 23. A method of controlling or treating diabetes in a mammal in need thereof comprising administering to the mammal a therapeutically effective amount of a compound of Claim 1 in combination with an insulin sensitizer or an insulin secretagogue.